

**REMARKS**

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The rejection of claims 1 and 9 under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,410,704 to Roizman et al. ("Roizman") is respectfully traversed in view of the above amendments and following remarks.

Roizman relates to the identification, purification and use of a herpes protease. Roizman solely discloses **viral** proteases; Roizman does not, however, disclose decreasing the levels of functional **cellular** protease in cells. Further, Roizman does not disclose calpain inhibitors. Accordingly, the rejection is improper and should be withdrawn.

The rejection of claim 18 under 35 U.S.C. §112(second paragraph) for indefiniteness is respectfully traversed in view of the above amendments.

The rejection of claims 1, 6-9 and 14-16 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is respectfully traversed.

In order for claims to be enabled, the specification, when filed, must contain sufficient information as to enable one skilled in the art to make and use the claimed invention. (Manual of Patent Examining Procedure ("MPEP") 2164.01). As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, the enablement requirement is satisfied. (In re Fisher, 427 F.2d. 833, 839, 166 USPQ 18, 24 (CCPA 1970); MPEP 2164.01(b)). In determining whether a patent application is in compliance with the enablement requirement, the PTO will consider whether one of ordinary skill in the art could practice the invention without undue experimentation. In re Wands, 858 F.2d. 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). Some experimentation may be required, as long as the experimentation is not undue.

The claims of the application set forth methods which decrease levels of functional cellular protease to decrease viral replication by a human cytomegalovirus, a herpes simplex virus, or a varicellar zoster virus by exposing the cells to a calpain inhibitor. These claims are fully enabled. These steps could be achieved by one of ordinary skill in the art without undue experimentation. As set out in the present application, cells are infected with a DNA virus, such as HCMV (specification, page 22, line 25- page 23, line 5). Contacting the cells with calpain inhibitors is disclosed (page 30, line 9- page 34, line 32). The specification fully discloses that HCMV infection decreases the abundance of p21<sup>cip1</sup> (page 26, line 29- page 28, line 12) and that calpain inhibitors protect p21<sup>cip1</sup> degradation during HCMV infection (page 30, line 9- page 34, line 12). In addition, the application shows that calpain is activated by HCMV infection (page 35, line 1- page 36, line 31) and that calpain cleaves p21<sup>cip1</sup> (page 37, line 1- page 38, line 20). Therefore, inhibitors of calpain inhibit the proteolysis of p21<sup>cip1</sup> (page 37, lines 21-22; Figure 19). Accordingly, the claims of the present application are enabled, because it is known that a decrease in the level of p21<sup>cip1</sup> is necessary for activation of E kinase activity and that activation of E kinase appears to be critical for efficient HCMV replication (page 3, lines 24-33).

In addition, although the application as filed contains these examples, compliance with the enablement requirement does not require applicants to provide a working example to enable one skilled in the art to practice the invention. (MPEP 2164.02). Further, where working examples are provided, the PTO, to make a valid rejection, must show why one would not be expected to extrapolate the example across the entire scope of the claims. (MPEP 2164.02).

Further, treating virally infected cells with inhibitors of cellular proteases and the measurement of the resultant viral infection is known in the art and described in the cited prior art. In particular, one of ordinary skill in

the art could readily ascertain whether viral replication was decreased, the unpredictability of the particular mechanism of replication notwithstanding. Lastly, measurement of the level (or activity) of a cellular protease, such as calpain, is described (specification, page 25, lines 7 - 33) and known in the art (See Potter, column 14, example 6). Thus, one of ordinary skill in the art could practice the present invention without undue experimentation with the information known in the art and contained in the specification. Further, as discussed by the PTO (see office action dated October 23, 2002, page 6), prior art is available which teaches one of ordinary skill in the art how to infect cells with a virus, contact the cell with an inhibitor and test to determine if viral replication is decreased.

It is the position of the PTO that these arguments do not address the enablement of the claimed methods (outstanding office action, page 8). Applicants are not arguing that the ability to measure the outcome of the method enables the method, applicants are arguing that one of ordinary skill in the art, with the information contained in the application, as filed, could practice the claimed method without undue experimentation. The PTO has argued that one skilled in the art would not be able to determine if a specific inhibitor worked for a particular virus (outstanding office action, page 6). Applicants submit that one skilled in the art could practice the method of the invention without undue experimentation, because one skilled in the art could expose cells to calpain inhibitors other than those specifically disclosed to determine if the cellular protease activity was decreased. The fact that one skilled in the art may have to undergo some experimentation does not defeat the enablement of the present application. "A extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." (MPEP 2164.06). A considerable amount of experimentation is permissible, if it is merely routine or if the specification provides a reasonable amount of guidance with respect to the direction in

which the experimentation should proceed. (MPEP 2164.06; (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Accordingly, the rejection of claims 1, 6-9 and 14-16 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is improper and should be withdrawn.

Applicants request that the Information Disclosure Statement submitted to the PTO on June 11, 2003 be acknowledged.

In view of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

December 16, 2003

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